# BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

## IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.**

## REMARKS

Claims 1, 9, 16, 18, 19, 27 and 37 have been amended and Claim 8 has been cancelled without prejudice. As such, Claims 1-5, 7 and 9-48 are pending.

### A. Amendments:

Claim 1 has been amended to clarify that the controlled-release matrix system includes a continuum of material and a controlled-release component finely dispersed throughout the matrix system. Support for amended Claim 1 can be found throughout the specification and more specifically at page 12, lines 13-21.

Claim 9 has been amended to be consistent with claim 1 and to depend from claim 7, in light of the cancellation of claim 8.

Claims 16, 18, 19, 27 and 37 have been amended to be consistent with Claim 1.

### B. The Invention:

The invention is directed to controlled-release glucosamine compositions and methods for treating conditions that will benefit from the administration of glucosamine, e.g., conditions having an inflammatory component such as arthritis, which are capable of maintaining an effective blood serum level of the glucosamine over a designated time period. The release rate can be controlled to maintain effective blood levels, but without exceeding a blood serum level of glucosamine that will affect an adverse change in glucose regulation. This is especially critical for diabetic patients that could benefit from the administration of glucosamine. As glucosamine is very soluble in water and digestive fluids, it will readily dissolve out of or diffuse out of known delivery systems. However, it has been found that a controlled-release can be obtained by dispersing the therapeutically effective amount of glucosamine in a continuous matrix system which has a suitable controlled-release

component, i.e., the high molecular weight cellulose polymer, finely dispersed throughout the continuous matrix.

**B. Rejections:**

**Rejections based on Murch et al.**

On page 5, paragraph 10, of the Office Action, Claims 1-5, 16, 17 and 27-34 were rejected under 35 U.S.C. §103(a) as being unpatentable over Murch, et al. (U.S. Pat. No. 6,046,179).

The three criteria that must be met in order to establish a *prima facie* case of obviousness includes:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings.
>
> Second there must be a reasonable expectation of success.
>
> Finally, the prior art reference (or references when combined) must teach or suggest all the claimed limitations. See MPEP §2142.

The teaching or suggestion to make the claimed combination (or modification) and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The initial burden is on the examiner to provide some suggestion of the desirability of doing what the inventor has done. "To support the conclusion that the claimed invention is directed to obvious subject matter, the reference must expressly or impliedly suggest the

claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references. *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985).

Thus, unless there is some suggestion or motivation contained within the reference to modify its teachings to provide a controlled-release composition, which includes the controlled-release matrix system having all the claim limitations, a *prima facie* case of obviousness cannot be established.

It is respectfully submitted that there is no suggestion or motivation in the Murch et al. reference to modify its teachings to provide the claimed compositions and methods. More specifically, there is no suggestion or motivation to disperse a therapeutically effective amount of glucosamine in a controlled-release matrix system, in which the system includes a continuum of material having a controlled-release component (i.e., at least on water soluble high molecular weight cellulose polymer) finely dispersed throughout the matrix system and in which the system is capable of releasing the glucosamine in an amount and at a rate sufficient to maintain an effective glucosamine blood serum level over a designated time period.

Murch et al. relates to a composition and method for treating inflammatory bowel disease (IBD). Murch et al. teach that the composition containing the N-acetylglucosamine can be delivered to the bowel directly in the form of a suppository or enema, or in the form of an orally ingestible time-release substance which can withstand degradation by the gastric acids of the stomach and can release the N-acetylglucosamine in the bowel or colon. (See Col. 2, lines 53-64). Thus, Murch et al. actually teach away from releasing glucosamine in an amount and at a rate sufficient to maintain an effective glucosamine blood serum level over a designated time period. Instead, Murch et al. teach an essentially instantaneous release after passing through the stomach, as opposed to a continuous release over time as claimed.

Murch et al. clearly teach such an instantaneous release by teaching that their time-release composition includes an enteric coating which allows the N-acetylglucosamine to pass through the low pH portion of the digestive track, i.e. the stomach, and release in the higher pH range of intestinal fluids. The enteric coating is pH controlled and remains in tact until it reaches the intestinal fluids, where it then dissolves and releases the N-acetylglucosamine. (See col. 4, lines 21-43). There is no teaching or suggestion of a sustained release composition which provides a substantially constant release of the active ingredient over time.

As such, Applicants respectfully submit that there is no teaching or suggestion by Murch et al. of the claimed matrix system which provides a controlled, e.g., substantially constant, glucosamine release rate over a designed time period. Therefore, it is respectfully requested that the rejections of Claims 1-5, 16, 17 and 27-34, in view of Murch et al., be withdrawn.

**Rejections based on Henderson et al., in view of Shell and McClain et al.**

On pages 5-7, paragraph 11, of the Office Action, Claims 1-5 and 7-48 were rejected under 35 U.S.C. §103(a) as being unpatentable over Henderson et al. (U.S. Pat. No. 5,364,845), in view of Shell (U.S. Pat. No. 5,582,837), in further view of McClain et al.

The Henderson et al. reference is merely directed to a therapeutic composition which includes glucosamine and salts thereof, in combination with chondroitin sulfate and soluble salts of manganese. There is no teaching or suggestion of a controlled-release matrix system, which contain a controlled-release component as claimed.

The Shell reference is directed to sustained release oral drug dosage forms that include a tablet or capsule having a plurality of particles which contain the drug dispersed in an alkyl cellulose. Shell teaches that the tablet or capsule should be highly soluble so that the

particles rapidly disperse in the stomach after the capsule is ingested. (See col. 5, lines 23-33).

In contrast, the compositions of the present invention rely on a continuous matrix having a controlled-release component finely dispersed throughout the matrix to provide a controlled release of the glucosamine component over a designated period of time, as opposed to a plurality of separate particles as taught by Shell.

As such, Shell actually teaches away from a composition that has a continuous matrix, and instead teaches a delivery system which includes a combination of separate particles. Moreover, there is no teaching or suggestion by Shell of a controlled-release glucosamine composition. As glucosamine is highly soluble in water and digestive fluids, it would leach or diffuse out of the small particles of Shell too rapidly to effectively control the release over significant periods of time. Thus, by teaching a system which includes a plurality of small particles, it would not be effective for delivering glucosamine at a controlled rate over a significant time period.

The McClain et al. reference is directed to the study of the hexosamine pathway and insulin resistance. McClain et al. teach that a side effect of excessive glucosamine administration can be an insulin resistance response. However, McClain et al. do not teach or even suggest methods or compositions for controlling the rate of glucosamine administration to avoid an insulin resistance response.

The prior art references must be considered as a whole and the examiner may not pick and choose from the various teachings within the references. The combination as a whole must render the claimed invention obvious in order to properly support an obviousness rejection. When read as a whole, Henderson et al., in view of Shell and further in view of McClain et al., do not teach or suggest the controlled-release compositions as claimed, which

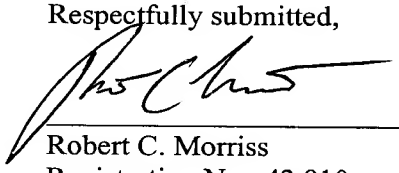
include a continuous matrix system for controlled delivery of glucosamine over a designated time period.

Accordingly, as none of the references taken separately or combined teach or suggest the presently claimed compositions or methods, it is respectfully requested that the rejections of Claims 1-5 and 7-48 be withdrawn.

## CONCLUSION

Accordingly, Applicants respectfully submit that the application as amended, including Claims 1-5, 7 and 9-48, is now in proper form for allowance, which action is earnestly solicited. If resolution of any remaining issue is required prior to examination of the application, it is respectfully requested that the Examiner contact Applicants' undersigned attorney at the telephone number provided below.

Respectfully submitted,



Robert C. Morriss
Registration No.: 42,910
Attorney for Applicant(s)

HOFFMANN & BARON, LLP
6900 Jericho Turnpike
Syosset, New York 11791
(516) 822-3550
RCM/jp

182052_1